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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/982,531	10/19/2001	Astrid Vrang	54320.000011	8179

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EXAMINER	
VOGEL, NANCY S	
ART UNIT	**PAPER NUMBER**
1636	

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05/03/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	09/982,531	VRANG ET AL.	
	Examiner	Art Unit	
	Nancy T. Vogel	1636	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *23 February 2007*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-11,14,17,24,27 and 30-45* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-11,14,17,24,27 and 30-45* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *2/23/07*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Claims 1-11, 14, 17, 24, 27, 30-45 are pending in the case.

Receipt of the Information Disclosure Statement on 2/23/07 is acknowledged.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-11, 14, 17, 24, 27, 30-45 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for methods of producing heterologous polypeptides or peptides or proteins in Lactococcus lactis, does not reasonably provide enablement for methods for producing heterologous polypeptides, peptides or proteins in any lactic acid bacteria. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

This rejection is maintained for reasons made of record in the previous Office action, mailed 10/23/06.

To recapitulate:

The factors considered when determining if the disclosure satisfies the enablement requirement and whether any necessary experimentation is undue include, but are not limited to: 1) nature of the invention, 2) state of the prior art, 3) relative skill of those in the art, 4) level of predictability in the art, 5) existence of working examples, 6) breadth of claims, 7) amount of direction or guidance by the inventor, and 8) quantity of experimentation needed to make or use the invention. *In re Wands*, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988).

The nature of the invention is a method of producing heterologous proteins in lactic acid bacteria, using chemically defined media and fed-batch or continuous cultivation.

The state of the prior art was advanced, in that methods of cell culture for the production of heterologous proteins was well known, although the field was well developed for use of such well known hosts as E. coli, but not for non-traditional recombinant hosts such as lactic acid bacteria.

The relative skill of those of those in the art was moderate, in that in general trial and error is used to determine optimal conditions for obtaining maximal amounts of a recombinant protein during cell culture.

The level of predictability of the art is very high, since it cannot be accurately predicted which growth media and conditions will result in maximal amounts of a recombinant protein in any particular cell type. For example, Jensen et al. (Appl. Environ. Microbiol. 59, 12, p. 4363-4366, 1993) disclosed that one particular lactic acid bacteria, Lactococcus lactis, has numerous growth requirements which required a particular combination of amino acids for sufficient growth, and that experimentation was required to determine appropriate conditions (page 4363). There is no expectation that the particular growth conditions needed for L. lactis would be appropriate for other types of lactic acid bacteria.

The existence of working examples in the specification is limited, since only methods using Lactococcus lactis are used.

The breadth of the claims is large, since the claims are drawn to methods using any lactic acid bacteria, and therefore encompasses all of the types of bacteria which includes such diverse organisms as defined in the specification, as follows: "Lactococcus spp., Streptococcus spp., Lactobacillus spp., Leuconostoc spp., Pediococcus spp., Brevibacterium spp. and Propionibacterium spp. Additionally, lactic acid producing bacteria belonging to the group 30 of the strictly anaerobic bacteria, bifidobacteria, ie Bifidobacterium spp., which are frequently used as food starter cultures alone or in combination with lactic acid bacteria, are generally included in the group of lactic acid bacteria" (page 6 of the specification).

The amount of guidance provided by the specification is limited, since the only guidance in the specification is limited to the disclosed method as applied to Lactococcus lactis.

Applicant's arguments filed 2/23/07 have been considered but have not been found convincing.

Applicants have argued that the chemically defined media for a wide range of lactobacilli and Pediococcus has been known for some time. Applicants submit several references to support the arguments which concern culture of Lactobacillus strains and

a Pediococcus strain. However, as was previously argued, unpredictability regarding the culture conditions for particular lactic acid bacteria exists, and experimentation is needed for the establishment of such culture conditions, for which guidance is not present in the specification. Furthermore, although applicants submit several references regarding Lactobacillus, and one regarding a Pediococcus strain, the lactic acid bacteria include diverse bacteria such as Streptococcus, Leuconostoc, Brevibacterium, and Propionibacterium. The claims are specifically directed to methods of cell culture for the production of heterologous proteins in the large group of bacteria encompassed by "lactic acid bacteria", and therefore the conditions must be known to practice the invention, and more than one example of one bacteria is necessary. Therefore, the rejection is maintained.

Claims 6, and 35 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

This rejection is maintained for reasons made of record in the previous Office action, mailed 10/23/06.

To recapitulate:

The rejection is based on the Guidelines for the Examination of Patent Applications under the 35 U.S.C. 112, first paragraph "Written Description published in the Federal Register (Volume 66, Number 4, Pages 1099-1111). Claim 6 and 35 are drawn to methods using a regulatable promoter which is "the P170 promoter disclosed

in WO 98/10079 or a derivative thereof". The specification has not defined what is encompassed by the term "derivative" and therefore it is given the broadest reasonable interpretation, and is interpreted to encompass any nucleotide sequence which is a regulatable promoter, since any nucleotide sequence can be derived from another by substitution, addition, or deletion. Claims 6 and 35 are genus claims in terms of a nucleotide sequence which functions as a regulatable promoter, which has an undefined structure or sequence. The disclosure is not deemed to be descriptive of the complete structure of a representative number of species encompassed by the claims as one of skill in the art cannot envision all DNA molecules which have regulatable promoter activity in the lactic acid bacteria and which are derived from the P170 promoter. While the specification provides general information on a particular promoter P170 and its structure and function, there is no disclosure of the precise nucleotides therein which could be modified by insertion, substitution or deletion and retain regulatable promoter activity in lactic acid bacteria. Therefore, the specification does not describe the claimed DNA in such full, clear, concise and exact terms so as to indicate that Applicant had possession of the product at the time of filing the present application. Thus the written description requirement has not been satisfied.

Applicant's arguments filed 2/23/07 have been considered but have not been found convincing.

Applicants have argued that the term "derivative" "can be any nucleotide sequence which is a regulatable promoter derived from another substitution, addition or deletion" and it "is not compatible with the dictionary meaning" (page 7). However, it is not disputed that this may be included in the meaning of the term "derivative" . However, it is maintained that the application has not provided an adequate written description of a sufficient number of species such that one can envision all the DNA molecules which have "regulatable" promoter activity in the lactic acid bacteria. There is no structure function analysis showing that the regions of the promoter needed for such activity were known, such that one would envision the variants with such activity. Therefore, the rejection is maintained.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 5 and 34 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

This rejection is maintained for reasons made of record in the previous Office action, mailed 10/23/06.

To recapitulate:

The claims are vague and indefinite in the recitation of "derived from a lactic acid bacterium", since "derived" is a term that is non-specific and relative in nature for which Applicant provides no definition. It provides no clarity as to what Applicant's claimed invention includes and what it does not include. Without a more specific definition, it is impossible to determine what and how may derivations comprise the invention. The nature and number of the derivations to arrive at the invention Applicant seeks to protect with the patent are not established such that a person skilled in the art would be apprised of the metes and bounds of the claims. The limits of the inventions cannot be discerned and others could not know if they were infringing Applicant's claim.

Applicant's arguments filed 2/23/07 have been considered but have not been found convincing.

Applicant has argued that the specification describes the promoter and derivation thereof from various sources. However, it is maintained that the term "derived" can include any modification or alteration, and it is not clear which modifications, alterations, are intended. Therefore the rejection is maintained.

Conclusion

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Nancy T. Vogel whose telephone number is (571) 272-0780. The examiner can normally be reached on 7:00 - 3:30, Monday - Friday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Joseph Woitach can be reached on (571) 272-0739. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

NV
4/29/07

NANCY VOCEL
PRIMARY EXAMINER